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General Summary

The integration of functions throughout the entire body is realized mainly through intercommunication via the nervous system. To understand how the activities of the organs affect brain activity and, in turn, how the brain controls the activities of the organs to optimize these integrative functions, it is absolutely necessary to clarify the mechanisms underlying the dynamic cell-to-cell signaling in the central nervous system underlying various specific functions, such as autonomic regulation and pain sensation. We use approaches at the molecular, cellular, and network levels, including patch-clamp recording of synaptic currents and real-time imaging of the intracellular Ca^{2+} concentration in living brain tissues from normal animals, animal models of various diseases, and animals with experimental manipulation of gene expression.

Research Activities

Central mechanisms of pain-related negative emotion

Using a rat model of chronic neuropathic pain, we demonstrated that structural consolidation is involved in synaptic potentiation at excitatory synapses between afferent fibers arising from the nucleus parabrachialis and neurons in the central nucleus of the amygdala, a structure playing a principal role in the expression of emotional behavior.

Glia-neuron interaction at central synapses

1. Astrocyte network activation through ATP receptors

In the nucleus of the solitary tract, we have demonstrated that astrocytes form a horizontally organized network with specific process extension and gap junction-mediated connections. We demonstrated that activation of P2Y1 receptors increases intracellular Ca concentrations at these processes, suggesting that processes, rather than the soma, are the functional units for glia-neuron interaction.

2. The role of monocarboxylate transport in the synaptic function

To clarify the role played by the transfer of lactate from astrocytes to neurons in synaptic transmission, we analyzed the effect of a selective inhibitor of monocarboxylate transporters on synaptic transmission in neurons of the nucleus of the solitary tract and found that lactate transport is needed to maintain the postsynaptic responses mediated by AMPA receptors, both in the presence and absence of glucose supply.

3. RNA interference modulation of presynaptic ATP receptor properties

To clarify the roles played by specific molecules in transmitter release in brain synapses, we developed a novel method for *in-vivo* gene silencing with RNA interference against the genes coding presynaptic proteins. We succeeded in altering pharmacological

characteristics of the presynaptic P2X receptors underlying extracellular ATP-evoked transmitter release, following reduced expression of subunit mRNA and protein by injection of small interfering RNA into the nodose ganglion.

Publications

Takahashi Y, Ikeda R, Kato F. Distinct mechanisms of synaptic potentiation in the central amygdala in distinct pain models (in Japanese). *Pain Res* 2009; **24:** 137–46.

Sumiyama, K, Tajiri, H, Kato F, Imura T, Ono K, Ikeda K, Imazu H, Gostout CJ. Pilot study for in vivo cellular imaging of the muscularis propria and *ex vivo*-molecular imaging of myenteric neurons. *Gastrointest Endosc* 2009; **69:** 1129–34.

Reviews and Books

Kato F. Synaptic mechanisms linkling chronic pain and emotion *Stress Sci* 2008; **23:** 23–35.

Kato F. Synaptic plasticity in the amygdala by chronic pain, Brain Science Review 2009, Eds Brain Science Foundation, Tokyo: Kubapuro; 2008. p. 163–79.